Complete Summary

GUIDELINE TITLE

Prostate cancer.

BIBLIOGRAPHIC SOURCE(S)

Singapore Ministry of Health. Prostate cancer. Singapore: Singapore Ministry of Health; 2000 May. 49 p. [168 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Prostate cancer

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Screening
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Oncology
Urology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide recommendations for the diagnosis, screening, management, and treatment of patients with prostate cancer

TARGET POPULATION

Asian men, 40 years of age and older

INTERVENTIONS AND PRACTICES CONSIDERED

Screening, diagnosis, and staging

1. Digital rectal examination
2. Measurement of prostate specific antigen (PSA) levels (Note: Prostate specific antigen velocity and prostate specific density are considered but not recommended.)
3. Transrectal ultrasound with and without guided prostate biopsy
4. Measurement of prostatic acid phosphatase and alkaline phosphatase (considered but not recommended for staging)
5. Pelvic lymph node dissection
6. Seminal vesicle biopsy (considered but not recommended for staging)
7. Computed tomography
8. Magnetic resonance imaging
9. Bone scan

Treatment

1. Surveillance
2. Radical prostatectomy
3. Radiotherapy, including 3-dimensional conformal radiotherapy (Note: Interstitial brachytherapy is considered but generally not recommended for locally advanced disease.)
4. Hormonal therapy, including orchiectomy, luteinizing hormone-releasing hormone (LHRH) analogue, diethylstilbestrol (DES), androgen suppression, and combined androgen blockade (combination of castration with an anti-androgen such as flutamide or bicalutamide).
5. Chemotherapy or chemo-hormonal therapy, such as mitoxantrone plus prednisolone and estramustine-based combinations (estramustine plus vinblastine, estramustine plus etoposide, estramustine plus paclitaxel)
6. Bisphosphonates, oral and intravenous analgesics and opiates, and radiotherapy for bone pain

Note: Other treatment options considered but not specifically recommended include adrenal androgen inhibitors (aminoglutethimide) plus replacement hydrocortisone; aminoglutethimide plus replacement hydrocortisone (or ketoconazole) plus flutamide withdrawal; other chemotherapeutic agents (doxorubicin, doxorubicin plus ketoconazole, estramustine plus doxorubicin, estramustine plus etoposide plus cisplatin or carboplatin); and suramin.

MAJOR OUTCOMES CONSIDERED

- Sensitivity, specificity, and positive predictive values of screening and diagnostic tests for prostate cancer
- Prostate specific antigen levels
- Size of measurable lesions or appearance of new measurable (e.g., soft tissue) lesions
- Pain associated with new bony (non-measurable) lesions
- Overall, progression-free, and disease-specific survival
- Palliation of symptoms (subjective response)

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Level Ia: Evidence obtained from meta-analysis of randomised controlled trials.

Level Ib: Evidence obtained from at least one randomised controlled trial.

Level IIa: Evidence obtained from at least one well-designed controlled study without randomisation.

Level IIb: Evidence obtained from at least one other type of well-designed quasi-experimental study.

Level III: Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.

Level IV: Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Workgroups comprising members from the Singapore Urological association and the Asian Society for Uro-oncology were formally appointed by the National Committee on Cancer Care to formulate clinical practice guidelines on urogenital cancers. The workgroup developing guidelines on the management of prostate cancer presented the draft to a panel of international and regional experts. All the relevant issues were discussed thoroughly till a consensus was achieved.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendation

Grade A (evidence levels Ia, Ib): Requires at least one randomized controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.

Grade B (evidence levels IIa, IIb, III): Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation.

Grade C (evidence level IV): Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates absence of directly applicable clinical studies of good quality.

Good Practice Points: Recommended best practice based on the clinical experience of the guideline development group.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Not stated

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Each recommendation is rated based on the level of the evidence and the grades of recommendation. Definitions of the grades of the recommendations (A, B, C, Good Practice Points) and level of the evidence (Level I - Level IV) are presented at the end of the Major Recommendations field.

Screening and Diagnosis

Screening

A - At present, screening is not recommended among Asians. (Grade A, Level Ia)

GPP - All males above 40 years of age with the risk factor of having a first degree relative with prostate cancer at young age (younger than 60 years) may be screened. (Good Practice Point)

Tests for Screening and Diagnosis of Prostate Cancer

Prostate Specific Antigen (PSA)

B - The appropriate threshold prostate specific antigen level for the detection of cancer of the prostate is 4.0 ng/mL (Smart, 1997; Gann, Hennekens, & Stampfer, 1995; Colberg, Smith, & Catalona, 1993; Labrie et al., 1992). (Grade B, Level IIb)

B - Clinically significant cancers are detected by testing (Catalona et al., 1993; Gann, Hennekens, & Stampfer, 1995; Smith, Humphrey, & Catalona, 1997). (Grade B, Level IIa)

C - Prostate specific antigen-based screening has induced a stage migration (Catalona et al., 1993; Farkas et al., 1998) but only very preliminary indications of improved survival are available (Smart, 1997). (Grade C, Level IV)

B - The ratio of free to total prostate specific antigen levels is recommended as the sensitivity and specificity of levels at 2 to 10 ng/ ml for detecting cancer of the prostate is higher. (Grade B, Level IIa) However, the optimal cut-off level is still being investigated (Bangma, et al., 1995; Catalona, Smith, Ornstein, 1997; Catalona et al, 1998).

Digital rectal examination

B - Digital rectal examination is recommended as the combination of digital rectal examination and prostate specific antigen test enhances early prostate cancer detection. (Grade B, Level IIa)

Transrectal ultrasound guided biopsy

A - Prostate biopsy is recommended for patients with abnormal prostate specific antigen results and/or suspicious digital rectal examination (Catalona et al., 1993; Catalona et al., 1994). (Grade A, Level Ib)

B - Transrectal ultrasound guided needle biopsy is a safe procedure with few major but frequent minor complications. The use of antibiotics for aerobic and anaerobic bacterial coverage is to be considered; little consensus is available on the most appropriate regimen (Rietbergen et al., 1997; Rodriguez & Terris, 1998). (Grade B, Level III)

B - Biopsy findings of high grade prostatic intraepithelial neoplasia (PIN grades 2 and 3) and invasive prostate cancer necessitate further investigations in patients who are candidates for radical treatment of localised prostate cancer (Davidson et al., 1995; Haggman et al., 1997). (Grade B, Level IIb)

Staging of Prostate Cancer

Note: The current staging and grading methods of prostate cancer can be found in Annex 1 of the original guideline document.

Investigations for Staging of Prostate Cancer

Digital Rectal Examination

B - This is not recommended as a precise staging modality as the finding may differ significantly from the actual pathological stage. Concurrent prostatic diseases like benign prostate hypertrophy, prostatitis, previous prostatic biopsy or surgery could make the assessment more difficult (Obek, 1999; Phillips & Thompson, 1991). (Grade B, Level III)

Prostate Specific Antigen

B - A serum prostate specific antigen level of less than 10 ng/ml indicates a lower risk of periprostatic spread and metastasis. An increased risk of extracapsular extension or seminal vesicle involvement and even distant metastasis may be indicated with prostate specific antigen levels of greater than or equal to 10 ng/ml. As a general guide, if prostate specific antigen is greater than 10 ng/ml, more than 50% have capsular penetration; if prostate specific antigen is greater than 50 ng/ml, the majority have pelvic lymph node involvement (Partin et al., 1997). (Grade B, Level IIb)

Transrectal Ultrasound

B - Transrectal ultrasound alone is of limited value for the staging of prostate cancer. (Rifkin et al., 1990; Smith et al., 1997) The increasing number of positive

biopsy cores and the presence of perineural invasion have negative prognostic implications (Partin et al., 1997). (Grade B, Level III)

Pelvic Lymph Node Dissection

B - This remains the most accurate method of assessing nodal metastasis. However, patients with low risk disease (prostate specific antigen less than 10 ng/ml, Gleason's sum less than 7 and stage T1c disease) have less than 5% chance of having lymph node involvement. As such, only high risk patients with stage T3c or node positive disease should be recommended for pelvic lymph node dissection before definitive treatment for localised prostate cancer (Partin et al., 1997; Stone, Stock, & Unger, 1995). (Grade B, Level IIb)

Seminal Vesicle Biopsy

B - This is not recommended as it does not add significantly to the combination of clinical staging, prostate specific antigen and Gleason score, which predicts seminal vesicle involvement to an acceptable degree (Partin et al., 1997). (Grade B, Level IIb)

Computed Tomography (CT) And Magnetic Resonance Imaging (MRI)

B - The current role of computed tomography and magnetic resonance imaging in the staging of localised prostate cancer is rather limited. Most of the microscopic features of extracapsular spread, seminal vesicle invasion and pelvic node metastasis are not obvious in radiological films. Interobserver variation has also been reported. However, there may be a role for computed tomography/magnetic resonance imaging in the staging of patients with high risk of nodal metastasis (Rifkin et al., 1990; Schiebler et al., 1992; Levran et al., 1995; Wolf et al., 1995; Li & Poon, 1988). (Grade B, Level III) Magnetic resonance imaging may also be useful in cases of high clinical suspicion of bone metastases with inconclusive bone scan or probable vertebral pathology leading to a spinal cord problem.

Bone Scan

B - This is the most sensitive method for detecting bone metastasis. However, in cases with prostate specific antigen less than 10 ng/ml, the probability of a positive scan is low in the absence of bone pain. Bone scans can be omitted in these patients. (Grade B, Level III)

Treatment of Localized Prostate Cancer

The choice of treatment between surveillance, surgery and radiation for localised prostate cancer should be individualized and based on an assessment of the biological potential of the disease, the life expectancy of the patient and the preference of the patient. There is no clear-cut evidence available showing definite advantage of one over the others.

Surveillance

B - The potential benefits of surveillance in patients with low grade, low volume tumour and elderly patients with limited life expectancy are the absence of complications compared to conventional radiotherapy or radical surgery and the minimal costs involved. (Grade B, Level III)

Radical Prostatectomy

B - An assessment of the biological potential of the disease, the life expectancy of the patient, the preferences of the patient and availability of expertise are important considerations in establishing the choice of therapy for localised prostate cancer (Zincke et al., 1994). The results of non-randomized retrospective reviews showed that 10 and 15 years actuarial survivals are 10 to 15% better after surgery than radiation or surveillance, particularly for the high-risk group, i.e., Gleason's sum greater than 6, stage T2c or prostate specific antigen less than 20 ng/ml ml (Pound et al., 1997; Blute et al., 1989; Lepor, Kimball, & Walsh, 1989; Montgomery et al., 1990; Catalona & Smith, 1998; D'Amico et al., 1998). (Grade B, Level III)

B - Patients with clinically organ-confined disease, relatively long life expectancy and no significant surgical risk factors are most likely to benefit from surgery (Partin et al., 1993). Young patients in the high-risk group may benefit from surgery. (Grade B, Level IIa)

B - In selected individuals with prolonged life expectancy, surgery may be offered for clinical stage T3 disease. (Grade B, Level III)

B - For patients with stage T1a and T1b disease, surgery is an option for patients less than 70 years of age with intermediate or high-risk disease, e.g., T1b with Gleason's sum greater than 5. The additional morbidity associated with radical prostatectomy after transurethral resection of prostate (TURP) should be considered (Gerber et al., 1996). (Grade B, Level III)

B - Gross locally advanced disease (e.g., presence of hydronephrosis), failure after radiation and patients with less than 10 years life expectancy are contraindications to radical prostatectomy (Paulson et al., 1988; Paulson, 1988). (Grade B, Level III)

B - As radical prostatectomy carries significant morbidity, a thorough evaluation of the patient's comorbidity and discussion of options are recommended. (Grade B, Level III)

B - Intraoperative pelvic lymph node dissection may be omitted in patients with low prostate specific antigen, low Gleason's score and clinically early disease (Dillioglugil et al., 1997a; Gerber et al., 1997; Partin et al., 1997). (Grade B, Level III)

B - Both perineal and retropubic prostatectomy give comparable results in terms of morbidity and disease-free survival (Dillioglugil et al., 1997b). (Grade B, Level III)

B - Neoadjuvant hormone therapy has not resulted in improved survival and is not recommended currently (Walsh, 1998; Cadeddu et al., 1998). (Grade B, Level IIb)

B - Prostate specific antigen levels should be taken at 4 to 6 weeks post-operation, followed by 6 monthly prostate specific antigen levels for 10 years, and yearly prostate specific antigen levels thereafter. Digital rectal examination should be performed at every visit. Bone scans, computed tomography scans and prostate bed biopsy are considered in the evaluation for salvage therapy. In the absence of raised prostate specific antigen, yield from imaging is negligible and not recommended. (Grade B, Level III)

Radiotherapy

B - Experience in the last 3 decades has demonstrated that radiotherapy is effective in the permanent control of prostatic tumours. (Grade B, Level IIa) However, as few patients undergo repeat biopsy of the gland to confirm response, the true incidence of local control may be lower than the 65 to 88% reported (Bagshaw et al., 1993; Hanks et al., 1987; Hanks et al., 1994; Perez, et al., 1993; Zagars et al., 1995; Zagars, 1994).

B - Long term results of radiotherapy in stage T1 and T2 patients are similar to those reported with radical prostatectomy despite differences in case selection and the lack of surgical staging of the lymph nodes in most cases. (Grade B, Level III) The definition of endpoints needs to be considered in non-randomised comparisons (Coleman et al., 1994).

A - Pelvic nodal irradiation does not confer any benefit in terms of local control or survival. (A, Level Ib) Pelvic nodal involvement is invariably associated with the development of distant metastases (Asbell et al., 1988; Leibel et al., 1994).

B - The data from trials (See Annex 2 in the original guideline document) suggest a role for the use of concurrent hormonal therapy with radiation for the treatment of localised prostate cancer. However, the type of androgen deprivation and its duration remains to be established (Bolla et al., 1997; Laverdiere et al., 1997; Pilepich et al., 1997). (B, Level III) Complications with radiotherapy for patients treated with neoadjuvant therapy may be lower.

B - Early reports have shown that 3-dimensional conformal radiotherapy (3D-CRT) may improve local control and survival in patients with prostate cancer (Hanks et al., 1997; Roach et al., 1996). (B, Level IIb) Post high dose radiotherapy morbidity may also be limited by this approach.

B - Interstitial brachytherapy is generally not recommended for locally advanced disease: prostate specific antigen greater than 10 ng/ml and high Gleason score (Blasko et al., 1995; Critz et al., 1996; Ragde et al., 1998; Wallner, Roy, & Harrison, 1996). (B, Level IIa)

A - To assess for post-treatment disease status, prostate specific antigen levels done 6-monthly for a period of 10 years and annually thereafter is recommended (Zagars, 1994; Critz et al., 1996; Ragde et al., 1998; Stock et al., 1996). (A,

Level Ib) Nadir prostate specific antigen levels (less than or equal to 0.5 ng/ml), typically achieved at 12 to 24 months, is of prognostic significance for relapse.

Management of Locally Advanced Prostate Cancer (Stage T3 N0 M0, T4 N0 M0, T1-4 N1 M0)

B - There is evidence that long-term survival is possible with control of locally advanced disease confined to the pelvis (Cox, 1993; Hanks et al., 1998). Endorectal coils for magnetic resonance imaging may enhance imaging of the prostate (Bartolozzi et al., 1996). (Grade B, Level III)

B - Androgen deprivation improves survival of patients with locally advanced prostate cancer. Neoadjuvant hormonal therapy reduces the radiation field size and hence treatment-related morbidity (Bolla et al., 1997; Laverdiere et al., 1997). (Grade B, Level III) The role of adjuvant hormonal therapy for locally advanced prostate cancer is currently being evaluated. Preliminary findings showed no survival advantage but significant disease-free interval for patients who had immediate orchiectomy (Fellows et al., 1992).

For asymptomatic patients, surveillance is an option.

Treatment for Locally Advanced (T3) Prostate Cancer

B - While the mainstay of treatment is systemic androgen deprivation therapy, local therapy in the form of radical prostatectomy with adjuvant radiotherapy, hormonal treatment or radiotherapy with hormonal adjuvant therapy may offer some benefit (Cheng et al;, 1993; Petrovich et al., 1998). (Grade B, Level III)

A - Neoadjuvant hormonal therapy before radical prostatectomy is not recommended as there is no obvious benefit (Lee et al., 1997). (Grade A, Level Ib)

Treatment for Locally Advanced (N+) Prostate Cancer

B - Radical prostatectomy with adjuvant hormonal therapy is advocated by some who reported good long-term survival (Cadeddu et al., 1997; Schmeller & Lubos, 1997; Seay, Blute, & Zincke, 1998; deKernion et al., 1990). (Grade B, Level III)

Biochemical Failure

B - Biochemical failure is defined as serum prostate specific antigen levels of 0.4 ng/ml following surgery, 0.5 ng/ml following radiotherapy, and/or 2 consecutive rising prostate specific antigen values 3 months apart. (Grade B, Level IIb) It is an elevation of, or consistently raised, prostate specific antigen level after definitive treatment indicating persistent local or systemic disease. It usually precedes clinical recurrence by up to 3 years (Pound et al., 1997; Lange et al., 1989; Goad et al., 1993).

B - Early elevated prostate specific antigen levels in less than 12 months post-treatment may indicate distant spread of disease. The prostate specific antigen level in this instance is also significantly higher than that in local recurrence. A

short prostate specific antigen doubling time or prostate specific antigen velocity of more than 0.75 ng/ml/year may indicate systemic recurrence (Cox, Kaplan, & Bagshaw, 1994; Fowler et al., 1994). (Grade B, Level III) Elevated prostate specific antigen levels more than 12 months post-treatment may indicate local recurrence.

Patients with biochemical failure need to be investigated for local or systemic recurrences.

B - Digital rectal examination is an unreliable early indicator of recurrence of local cancer following treatment (Lightner et al., 1990). (Grade B, Level III)

B - Transrectal ultrasound is of no value in the diagnosis of local disease after treatment when it is used independently. However, transrectal ultrasound has a definite role in facilitating localisation and guiding systematic biopsy for patients with elevated prostate specific antigen and/or suspicious digital rectal examination (Abi-Aad et al., 1992; Goldenberg et al., 1992; Kabalin et al., 1989; Kapoor et al., 1993). (Grade B, Level III)

Bone scan may be indicated to detect systemic bony metastasis although elevated prostate specific antigen levels may precede positive bone scans by a median of 10 months (Lightner et al., 1990; Terris et al., 1991).

B - Computed tomography/magnetic resonance imaging of the abdomen and pelvis may be indicated in evaluating post-prostatectomy patients for adjuvant radiation with elevated prostate specific antigen levels, normal bone scan, normal transrectal ultrasound and biopsy (Hricak et al., 1987). (Grade B, III)

GPP - ProstaScint scan may enhance identification of systemic recurrence after treatment (Elgamal, Troychak, & Murphy, 1998). (Good Practice Point)

Treatment of Metastatic Prostate Cancer (M1)

The presence of disease in non-pelvic lymph nodes, bone or distant (other than pelvis) sites constitutes the definition of M1/D2 disease The presence of visceral or lytic metastatic lesions should alert clinicians of variant histology (e.g., neuroendocrine tumour). (Grade A, Level Ia)

First line treatment

B - Early treatment improves local and distant disease control. (Grade B, Level Ib*)

A - The different treatment modalities - orchiectomy, luteinizing hormone-releasing hormone (LHRH) analogue and diethylstilbestrol (DES) - though differing in toxicity and costs, give equivalent results (The Leuprolide Study Group, 1984; Kaisary et al., 1991; Peeling, 1989; Vogelzang et al., 1995). (Grade A, Level Ib)

A - Total androgen blockage is not recommended presently. (Grade A, Level Ia)

B - Total androgen blockage may be indicated under some special circumstances:

- Flare prevention during first month of luteinizing hormone-releasing hormone agonist therapy
- Severe symptoms, as faster relief is associated with initial total androgen blockage
- As second-line therapy (McLeod et al., 1993; Parmar et al., 1987) (Grade B, Level IIb)

B - Intermittent androgen suppression is currently experimental, (Grade B, Level III) although there are certain encouraging animal and phase II study results. It is associated with lower costs and improved quality of life (sense of well being, recovery of libido and potency). Currently, phase III trials are ongoing (Akakura et al., 1993; Goldenberg, et al., 1995; Klotz et al., 1986; Oliver et al., 1997).

A - Monotherapy with bicalutamide or finasteride is, at present, not recommended. (Grade A, Level Ib)

Second line treatment

A - First line treatment, whether monotherapy or combined androgen blockade, usually controls disease for only 12 to 18 months and second line treatment is very often necessary (Prostate Trialists' Collaborative Group, 1995; Crawford et al., 1989; Eisenberger et al., 1998; Waselenko & Dawson, 1997). (Grade A, Level Ib)

A - None of the second line treatment options has shown consistent advantage. The choice of treatment should again be individualized. (Grade A, Level Ib)

GPP - For patients who are using only luteinizing hormone-releasing hormone agonist or oestrogen as primary therapy but whose testosterone level is not below castration level (defined as the limit of detection in individual laboratories), adding an anti-androgen is useful. (Good Practice Point)

B - Patients who are using only luteinizing hormone-releasing hormone agonist or oestrogen as primary therapy but whose testosterone level is at castration level may benefit from indefinite use of luteinizing hormone releasing-hormone agonist. (Grade B, Level III)

B - For patients who are using anti-androgens or combined androgen blockade, anti-androgen withdrawal is the preferred approach. (Grade B, Level IIa) It may be useful to continue prescribing luteinizing hormone releasing-hormone agonist indefinitely once it has been started even in relapse cases. However, data on this issue is conflicting (Hussain et al., 1994; Taylor, Elson, & Trump, 1993).

B - The withdrawal benefits of megestrol acetate, a progesterone agent that acts centrally as well as at the androgen receptor, has also been reported (Dawson et al., 1997). (Grade B, Level IIb)

Supportive care with prednisolone

A - Low-dose glucocorticoids (e.g., prednisolone 10 mg daily) are effective and achieve reasonable palliative relief for patients who are not fit for aggressive chemotherapy (Tannock et al., 1996). (Grade A, Level Ib)

B - Low dose prednisolone is probably as effective as the addition of flutamide as a second-line therapy (Datta, Thomas, & Matthews, 1997). (Grade B, Level IIa)

Chemotherapy or Chemo-hormonal Therapy

Mitoxantrone plus prednisolone (M plus P)

B - Mitoxantrone plus prednisolone combination is USFDA (United States Food and Drug Administration) approved. In a Canadian trial, it produced a 29% response rate with palliation of pain as the endpoint, as well as a longer duration of palliation. The result was better than that of using prednisolone alone (12% response rate with similar endpoint). The survival benefit was possibly due to a cross-over design (Tannock et al., 1996). (Grade B, Level Ib*)

Estramustine plus estramustine-based combinations

B - Oral estramustine alone produced 19% objective response rate in 18 phase II trials. Estramustine (10 to 15 mg/kg po daily) plus vinblastine (3 to 4 mg/m2 IV weekly) produced 40% objective response rate and 54% prostate specific antigen response in phase II studies. Estramustine plus vinblastine combination was superior to vinblastine alone in a phase III study (Eisenberger et al., 1998; Benson & Hartley-Asp, 1990; Hudes et al., 1992; Hudes et al., 1997; Seidman et al., 1992). (Grade B, Level IIb) Estramustine (15 mg/kg po daily) plus etoposide (50 mg/m2 po daily) for 21 days out of 28 days is an active combination. Estramustine plus paclitaxel (120 mg/m2 over 96 hours) combination every 21 days. Two drugs that impair microtubule function by complementary mechanisms (Hudes et al., 1997).

Treatment for Bone Pain

Radiotherapy

External beam irradiation is indicated for painful bony metastases, or unstable bony metastases.

Hemibody irradiation is indicated for patients who have too many symptomatic bony metastases to be treated individually.

Radioisotopes such as Strontium-89 and Samarium-153 are beta-emitting isotopes which can improve bone pain in up to 70% of treated patients. However, this may cause myelosuppression, especially if chemotherapy is subsequently needed (Porter et al., 1993).

Bisphosphonates

B - Bisphosphonates can reduce bone pain in up to 76% of treated patients (Pelger et al., 1998). (Grade B, Level IIb)

Pain service

The availability of a pain service to co-ordinate the use of oral and intravenous analgesics and opiates is encouraged.

*Although the trial reported is of a higher level of evidence, the grade accorded is lower as the workgroup is of the opinion that more research in the area needs to be done.

Grades of Recommendation

Grade A (evidence levels Ia, Ib): Requires at least one randomized controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.

Grade B (evidence levels IIa, IIb, III): Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation.

Grade C (evidence level IV): Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates absence of directly applicable clinical studies of good quality.

Good Practice Points: Recommended best practice based on the clinical experience of the guideline development group.

Levels of Evidence

Level Ia: Evidence obtained from meta-analysis of randomised controlled trials.

Level Ib: Evidence obtained from at least one randomised controlled trial.

Level IIa: Evidence obtained from at least one well-designed controlled study without randomisation.

Level IIb: Evidence obtained from at least one other type of well-designed quasi-experimental study.

Level III: Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.

Level IV: Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- The potential benefits of surveillance in patients with low grade, low volume tumour and elderly patients with limited life expectancy are the absence of complications compared to conventional radiotherapy or radical surgery and the minimal costs involved.
- With the widespread use of prostate specific antigen, more patients are found with organ-confined disease, and curative measures by surgical removal of cancer can be achieved. Surgery also offers more accurate staging, allowing better planning for adjuvant therapy.
- Results of non-randomized retrospective reviews showed that 10 and 15 years actuarial survivals are 10 to 15% better after surgery than radiation or surveillance, particularly for the high-risk group (i.e., Gleason's sum greater than 6, stage T2c, or prostate specific antigen les than 20 ng/mL.
- Hormonal therapy achieved favorable response in 75 to 80% of patients with advanced prostate cancer. The median duration of response is 18 months and the median survival time in 30/36 months.

Subgroups Most Likely to Benefit:

Patients with clinically organ-confined disease, relatively long life expectancy and no significant surgical risk factors are most likely to benefit from surgery. Young patients in the high-risk group may benefit from surgery.

POTENTIAL HARMS

Transrectal ultrasound guided needle biopsy

Transrectal ultrasound guided needle biopsy is a safe procedure with few major but frequent minor complications.

Prostatectomy

As radical prostatectomy carries significant morbidity, a thorough evaluation of the patient´s co-morbidity and discussion of options are recommended. Short-term morbidity includes intraoperative bleeding, rectal injury, pulmonary embolism, myocardial infarction and infective complications. Long-term morbidity includes incontinence, impotence and bladder neck contracture. Erectile dysfunction is common even after nerve sparing procedures. Overall morbidity may be higher than that reported from large institutions.

Radiotherapy

The late complications of radiotherapy include chronic mild-to moderate cystitis (12.5%), diarrhoea (9.7%), proctitis (7.8%), rectal bleeding (4.4%), urethral stricture or bladder neck contracture (3%) and haematuria (3%). Severe complications are rare. Complications with radiotherapy for patients treated with neoadjuvant therapy may be lower.

Hormone therapy

Hormone-associated toxicity includes osteoporosis, hot flushes, sexual dysfunction (decreased libido), gynaecomastia, nausea, vomiting, diarrhoea, insomnia and lethargy.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

These guidelines are not intended to serve as standards of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

The contents of the guideline document are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient in the light of the clinical data presented by the patient and the diagnostic and treatment options available.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Assessing treatment responses

Given the different treatment endpoints in prostate cancer, it is necessary to report and analyse treatment data based on individual endpoints. Accepted treatment endpoints in prostate cancer are:

For metastatic disease:

i. objective response of measurable disease
ii. prostate specific antigen response
iii. subjective response

For local-regional disease:

i. progression-free survival

ii. disease-specific survival
iii. overall survival

One of the most robust treatment endpoints in prostate cancer is survival. In this regard, the overall survival is probably more reliable than disease-specific survival since documentation of the cause of deaths in prostate cancer is often not reliable.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Singapore Ministry of Health. Prostate cancer. Singapore: Singapore Ministry of Health; 2000 May. 49 p. [168 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 May

GUIDELINE DEVELOPER(S)

National Committee on Cancer Care (Singapore) - National Government Agency [Non-U.S.]
National Medical Research Council (Singapore Ministry of Health) - National Government Agency [Non-U.S.]
Singapore Ministry of Health - National Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Ministry of Health appointed the National Committee on Cancer Care (NCCC) in January 1998 to advise on the formulation of policies on cancer services in Singapore.

Workgroups comprising members from the Singapore Urological Association and the Asian Society for Uro-oncology were formally appointed by the National Committee on Cancer Care to formulate clinical practice guidelines on the management of urogenital cancers.

SOURCE(S) OF FUNDING

Singapore Ministry of Health

GUIDELINE COMMITTEE

National Committee on Cancer Care Workgroup on Prostate Cancer

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Workgroup members. Dr. Christopher Cheng (Chairperson); Dr. Christopher Chee; Dr. Chia Sing Joo; Dr. Kong Hwai Loong; Dr. Lewis Liew; Dr. Robert Lim; Dr. Ng Foo Cheong; Dr. Ng Lay Guat; Dr. Damian Png; Dr. Terence Tan; Dr. Tan Puay Hoon; Dr. Tan Yeh Hong; Dr. Toh Khai Lee; Dr. Karmen Wong; Dr. Yang Tuck Loong; Dr. Sidney Yip.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

An update is not in progress at this time.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Singapore Ministry of Health Web site.

Print copies: Available from the Singapore Ministry of Health, College of Medicine Building, Mezzanine Floor 16 College Rd, Singapore 169854.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on October 25, 2001. The information was verified by the guideline developer on November 16, 2001.

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